

AMENDMENTS TO THE SPECIFICATION:

Please replace the section on page 3, lines 6-10 with the following amended section: (insertions are underlined, deletions are in ~~strikethrough~~):

R₄ is selected from hydrogen, F, Cl, Br, CN, -OR₁₆, -SR₁₆, an optionally substituted alkyl, an optionally substituted alkenyl, an optionally substituted alkynyl, an optionally substituted haloalkyl, ~~[[and]]~~ an optionally substituted heteroalkyl, an optionally substituted aryl, an optionally substituted heteroaryl, an optionally substituted heterocyclyl and an optionally substituted cycloalkyl; or

Please replace the section on page 3, lines 26-27 with the following amended section:

R₆ is selected from hydrogen, F, Cl, Br, an optionally substituted alkyl, an optionally substituted alkenyl, and an optionally substituted alkynyl;

Please replace the section on page 4, lines 9-12 with the following amended section:

R₇ and R₈ together form an optionally substituted 5-6 member ring and R₉ is selected from hydrogen, F, Cl, Br, CN, an optionally substituted alkyl, an optionally substituted alkenyl, an optionally substituted alkynyl, an optionally substituted haloalkyl, and an optionally substituted heteroalkyl, or

Please replace the section on page 4, lines 18-19 with the following amended section:

R₁₀ is selected from hydrogen, F, Cl, Br, an optionally substituted alkyl, an optionally substituted alkenyl, and an optionally substituted alkynyl; and

Please replace the section on page 5, lines 27-28 with the following amended section:

R₁₇ is selected from ~~hydrogen~~ hydrogen, ~~[[and]]~~ an optionally substituted alkyl, an optionally substituted alkenyl and an optionally substituted alkynyl;

Please replace the section on page 5, line 29 through page 7, line 11 with the following amended section:

wherein the substituents on the alkyl, alkenyl, alkynyl, aryl, heteroaryl, heterocyclyl and cycloalkyl groups, when present are selected from one or more, in certain embodiments, 1 to 4, in other embodiments, 1, 2 or 3 substituents, each independently selected from Q¹, wherein Q¹ is halo, pseudohalo, hydroxy, oxo, thia, nitrile, nitro, formyl, mercapto, hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl, aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkyl diarylsilyl, triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxycarbonyl, alkoxycarbonylalkyl, aryloxy carbonyl, aryloxy carbonylalkyl, aralkoxycarbonyl, aralkoxycarbonylalkyl, arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy, aryloxy, heteroaryloxy, heteroaralkoxy, heterocyclyloxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyloxy, aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, alkoxycarbonyloxy, aryloxy carbonyloxy, aralkoxycarbonyloxy, aminocarbonyloxy, alkylaminocarbonyloxy, dialkylaminocarbonyloxy, alkylarylaminocarbonyloxy, diarylaminocarbonyloxy, guanidino, isothioureido, ureido, N-alkylureido, N-arylureido, N'-alkylureido, N',N'-dialkylureido, N'-alkyl-N'-arylureido, N',N'-diarylureido, N'-arylureido, N,N'-dialkylureido, N-alkyl-N'-arylureido, N-aryl-N'-alkylureido, N,N'-diarylureido, N,N',N'-trialkylureido, N,N'-dialkyl-N'-arylureido, N-alkyl-N',N'-diarylureido, N-aryl-N',N'-dialkylureido, N,N'-diaryl-N'-alkylureido, N,N',N'-triarylureido, amidino, alkylamidino, arylamidino, imino, hydroxyimino, alkoxyimino, aryloxyimino, aralkoxyimino, alkylazo, arylazo, aralkylazo, aminothiocarbonyl, alkylaminothiocarbonyl, arylaminothiocarbonyl, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl, alkylarylaminominoalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diarylamino, alkylarylaminomino, alkylcarbonylamino, alkoxycarbonylamino, aralkoxycarbonylamino, arylcarbonylamino, arylcarbonylaminoalkyl, aryloxy carbonylaminoalkyl, aryloxyarylcarbonylamino, aryloxy carbonylamino, alkylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino, heterocyclylsulfonylamino, heteroarylthio, azido, -N⁺R⁵¹R⁵²R⁵³, P(R⁵⁰)₂, P(=O)(R⁵⁰)₂, ~~OP(=O)(R⁵⁰)₂~~ OP(=O)(R⁵⁰)₂, -NR⁶⁰C(=O)R⁶³, dialkylphosphonyl, alkylarylphosphonyl, diarylphosphonyl,

hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio, hydroxycarbonyl-alkylthio, thiocyano, isothiocyano, alkylsulfinyloxy, alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy, hydroxysulfonyloxy, alkoxysulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy, dialkylaminosulfonyloxy, arylaminosulfonyloxy, diarylaminosulfonyloxy, alkylarylaminosulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxysulfonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl, diarylaminosulfonyl or alkylarylaminosulfonyl; or two Q¹ groups, which substitute atoms in a 1,2 or 1,3 arrangement, together form alkylenedioxy (*i.e.*, -O-(CH₂)_y-O-), thioalkylenoxy (~~*i.e.*, -S-(CH₂)_y-O-~~) or (*i.e.*, -S-(CH₂)_y-O-) or alkylenedithioxy (*i.e.* -S-(CH₂)_y-S-) where y is 1 or 2; or two Q¹ groups, which substitute the same atom, together form alkylene; and

Please replace the section on page 7, line 15 through page 8, line 25 with the following amended section:

each Q² is independently halo, pseudohalo, hydroxy, oxo, thia, nitrile, nitro, formyl, mercapto, hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl, aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkylarylsilyl, triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxycarbonyl, alkoxycarbonylalkyl, aryloxy carbonyl, aryloxy carbonylalkyl, aralkoxycarbonyl, aralkoxycarbonylalkyl, arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy, aryloxy, heteroaryloxy, heteroaralkoxy, heterocycloxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyloxy, aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, alkoxycarbonyloxy, aryloxy carbonyloxy, aralkoxycarbonyloxy, aminocarbonyloxy, alkylaminocarbonyloxy, dialkylaminocarbonyloxy, alkylarylaminocarbonyloxy, diarylaminocarbonyloxy, guanidino, isothioureido, ureido, N-alkylureido, N-arylureido, N'-alkylureido, N',N'-dialkylureido, N'-alkyl-N'-arylureido, N',N'-diarylureido, N'-arylureido, N,N'-dialkylureido, N-alkyl-N'-arylureido, N-aryl-N'-alkylureido, N,N'-diarylureido, N,N',N'-trialkylureido, N,N'-dialkyl-N'-arylureido, N-alkyl-N',N'-diarylureido, N-aryl-N',N'-dialkylureido, N,N'-diaryl-N'-alkylureido, N,N',N'-triarylureido, amidino, alkylamidino, arylamidino, imino, hydroxyimino, alkoxyimino, aryloxyimino, aralkoxyimino, alkylazo, arylazo, aralkylazo, aminothiocarbonyl, alkylaminothiocarbonyl,

arylaminothiocarbonyl, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl, alkylarylaminomethyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diarylamino, alkylarylaminomethyl, alkylcarbonylamino, alkoxy carbonylamino, aralkoxy carbonylamino, arylcarbonylamino, arylcarbonylaminoalkyl, aryloxy carbonylaminoalkyl, aryloxyarylcarbonylamino, aryloxy carbonylamino, alkylsulfonylamino, arylsulfonylamino, heteroaryl sulfonylamino, heterocyclylsulfonylamino, heteroarylthio, azido, $-N^+R^{51}R^{52}R^{53}$, $P(R^{50})_2$, $P(=O)(R^{50})_2$, $OP(=O)(R^{50})_2$, $OP(=O)(R^{50})_2$, $-NR^{60}C(=O)R^{63}$, dialkylphosphonyl, alkylarylphosphonyl, diarylphosphonyl, hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio, hydroxylcarbonyl-alkylthio, thiocyanomethyl, isothiocyanomethyl, alkylsulfinyloxy, alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy, hydroxysulfonyloxy, alkoxy sulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy, dialkylaminosulfonyloxy, arylaminosulfonyloxy, diarylamino sulfonyloxy, alkylarylaminosulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxy sulfonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl, diarylamino sulfonyl or alkylarylaminosulfonyl; or two Q^2 groups, which substitute atoms in a 1,2 or 1,3 arrangement, together form alkylene dioxy (*i.e.*, $-O-(CH_2)_y-O-$), thioalkyleneoxy (*i.e.*, $-S-(CH_2)_y-O-$) or (*i.e.*, $-S-(CH_2)_y-O-$) or alkylene dithiooxy (*i.e.* $-S-(CH_2)_y-S-$) where y is 1 or 2; or two Q^2 groups, which substitute the same atom, together form alkylene;

Please replace the paragraph beginning on page 10, line 29 with the following amended paragraph:

In certain embodiments, provided herein are methods for treating a subject evidencing a glucocorticoid receptor mediated disease or disorder, or a disease or disorder in which the activity of a glucocorticoid receptor is implicated by administering to the subject a compound provided herein.

Please replace the paragraph beginning on page 11, line 3 with the following amended paragraph:

In practicing the methods, effective amounts of the compounds or compositions containing therapeutically effective concentrations of the compounds, which are formulated for systemic delivery, including parenteral, oral, or intravenous delivery, or for local or topical application, for the treatment of glucocorticoid receptor mediated diseases or disorders, or diseases or disorders in which the activity of a glucocorticoid receptor is

implicated, including, but not limited to, inflammatory diseases, autoimmune diseases, hyperproliferative diseases, and other such disease. Exemplary of these diseases are inflammatory diseases, such as rheumatoid arthritis, asthma (acute and/or chronic), lupus, osteoarthritis, rhinosinusitis, inflammatory bowel disease, polyarteritis nodosa, Wegener's granulomatosis, giant cell arteritis, allergic rhinitis, urticaria, hereditary angioedema, chronic obstructive pulmonary disease, tendonitis, bursitis, autoimmune chronic active hepatitis, cirrhosis, transplant rejection, psoriasis, dermatitis, autoimmune disorders, malignancies (e.g., leukemia, myelomas, lymphomas), acute adrenal insufficiency, congenital adrenal hyperplasia, rheumatic fever, granulomatous disease, immune proliferation/~~apoptosis~~apoptosis, hypothalamic-pituitary-adrenal (HPA) axis suppression and regulation, hypercortisolemia, modulation of the Th1/Th2 cytokine balance, chronic kidney disease, stroke and spinal cord injury, hypercalcemia, hyperglycemia, cerebral edema, thrombocytopenia, Little's syndrome, Addison's disease, cystic fibrosis, myasthenia gravis, autoimmune hemolytic anemia, uveitis, pemphigus vulgaris, multiple sclerosis, nasal polyps, sepsis, infections (e.g., bacterial, viral, rickettsial, parasitic), type II diabetes, obesity, metabolic syndrome, depression, schizophrenia, mood disorders, Cushing's syndrome, anxiety, sleep disorders, memory and learning enhancement, or glucocorticoid-induced glaucoma[[,]]. Effective amounts of the compounds or compositions containing therapeutically effective concentrations of the compounds are administered to an individual exhibiting the symptoms of these diseases or disorders. The amounts are effective to ameliorate or eliminate one or more symptoms of the diseases or disorders.

Please replace the paragraph beginning on page 12, line 17 with the following amended paragraph:

Unless defined otherwise, all technical and scientific terms used herein have the same meaning as is commonly understood by one of skill in the art to which the claimed subject matter belongs. All patents, patent applications, published applications and publications, Genbank sequences, websites and other published materials referred to throughout the entire disclosure herein, unless noted otherwise, are incorporated by reference in their entirety. In the event that there are a plurality of definitions for terms herein, those in this section prevail. Where reference is made to a URL or other such identifier or address, it is understood that such identifiers can change and particular information on the internet can come and go, but equivalent information can be found by searching the internet. Reference thereto evidences

the availability and public dissemination of such ~~information.~~ It information. It is to be understood that both the foregoing general description and the following detailed description are exemplary and explanatory only and are not restrictive of the products, methods and other subject matter provided herein. In this application, the use of the singular includes the plural unless specifically stated otherwise. In this application, the use of "or" means "and/or" unless stated otherwise. Furthermore, use of the term "including" as well as other forms, such as "includes," and "included," is not limiting.

Please replace the paragraph beginning on page 14, line 9 with the following amended paragraph:

As used herein, the terms "treating" or "treatment" encompass either or both responsive and prophylaxis measures, e.g., designed to inhibit or delay the onset of the disease or disorder, achieve a full or partial reduction of the symptoms or disease state, and/or to alleviate, ameliorate, lessen, or cure the disease or disorder and/or its symptoms. Treatment also encompasses any pharmaceutical use of the compositions herein, such as use for treating ~~[[a]]~~ glucocorticoid mediated diseases or disorders.

Please replace the paragraph beginning on page 16, line 19 with the following amended paragraph:

As used herein, the term "lower alkyl" refers to an alkyl containing 1 to 5 carbon atoms. The term "medium alkyl" refers to an alkyl containing 5 to 10 carbon atoms. An alkyl can be designated as "C₁-C₄ alkyl" or similar designations. By way of example only, "C₁-C₄ alkyl" indicates an alkyl having one, two, three, or four carbon atoms, i.e., the alkyl is selected from among methyl, ethyl, propyl, iso-propyl, n-butyl, iso-butyl, sec-butyl, and t-butyl. This C₁ – C₄ includes C₁ – C₂ and C₁ – C₃ alkyl.~~[[.]]~~ Alkyls can be substituted or unsubstituted. Alkyls include, but are not limited to, methyl, ethyl, propyl, isopropyl, butyl, isobutyl, tertiary butyl, pentyl, hexyl, ethenyl, propenyl, butenyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and the like, each of which can be optionally substituted.

Please replace the paragraph beginning on page 22, line 6 with the following amended paragraph:

Unless otherwise indicated, the term "optionally substituted," refers to a group in which none, one, or more than one of the hydrogen atoms has been replaced with one or more

group(s) individually and independently selected from: cycloalkyl, aryl, heteroaryl, non-aromatic heterocycle, hydroxy, alkoxy, aryloxy, mercapto, alkylthio, arylthio, cyano, halo, carbonyl, thiocarbonyl, O-carbamyl, N-carbamyl, O-thiocarbamyl, N-thiocarbamyl, C-amido, N-amido, S-sulfonamido, N-sulfonamido, C-carboxy, O-carboxy, isocyanato, thiocyanato, isothiocyanato, nitro, silyl, trihalomethanesulfonyl, and amino, including mono and di substituted amino groups, and the protected derivatives of amino groups. ~~Such groups. Such~~ protective derivatives (and protecting groups that can form such protective derivatives) are known to those of skill in the art and can be found in references such as Greene and Wuts, above. In embodiments in which two or more hydrogen atoms have been substituted, the substituent groups can together form a ring.

Please replace the paragraph beginning on page 23, line 1 with the following amended paragraph:

As used herein, a “prodrug” refers to ~~[[an]]~~ a pharmaceutical agent that is converted from a less active form into a corresponding more active form *in vivo*. A prodrug is a compound that, upon *in vivo* administration, is metabolized by one or more steps or processes or otherwise converted to the biologically, pharmaceutically or therapeutically active form of the compound. To produce a prodrug, the pharmaceutically active compound is modified such that the active compound will be regenerated by metabolic processes. The prodrug can be designed to alter the metabolic stability or the transport characteristics of a drug, to mask side effects or toxicity, to improve the flavor of a drug or to alter other characteristics or properties of a drug. By virtue of knowledge of pharmacodynamic processes and drug metabolism *in vivo*, those of skill in this art, once a pharmaceutically active compound is known, can design prodrugs of the compound (see, *e.g.*, Nogrady (1985) *Medicinal Chemistry A Biochemical Approach*, Oxford University Press, New York, pages 388-392).

Please replace the paragraph beginning on page 23, line 21 with the following amended paragraph:

As used herein, pharmaceutically acceptable derivatives of a compound include salts, esters, enol ethers, enol esters, acetals, ketals, orthoesters, hemiacetals, hemiketals, acids, bases, solvates, hydrates or prodrugs thereof. Such derivatives can be readily prepared by those of skill in this art using known methods for such derivatization. The compounds

produced can be administered to animals or humans without substantial toxic effects and either are pharmaceutically active or are prodrugs. Pharmaceutically acceptable salts include, but are not limited to, amine salts, such as but not limited to N,N'-dibenzylethylenediamine, chloroprocaine, choline, ammonia, diethanolamine and other hydroxyalkylamines, ethylenediamine, N-methylglucamine, procaine, N-benzylphenethylamine, 1-para-chlorobenzyl-2-pyrrolidin-1'-ylmethylbenzimidazole, diethylamine and other alkylamines, piperazine and tris(hydroxymethyl)aminomethane; alkali metal salts, such as but not limited to lithium, potassium and sodium; alkali earth metal salts, such as but not limited to barium, calcium and magnesium; transition metal salts, such as but not limited to zinc; and other metal salts, such as but not limited to sodium hydrogen phosphate and disodium phosphate; and also including, but not limited to, salts of mineral acids, such as but not limited to hydrochlorides and sulfates; and salts of organic acids, such as but not limited to acetates, lactates, malates, tartrates, citrates, ascorbates, succinates, butyrates, valerates and fumarates. Pharmaceutically acceptable esters include, but are not limited to, alkyl, alkenyl, alkynyl, aryl, heteroaryl, aralkyl, heteroaralkyl, cycloalkyl and heterocyclyl esters of acidic groups, including, but not limited to, carboxylic acids, phosphoric acids, phosphinic acids, sulfonic acids, sulfinic acids and boronic acids. Pharmaceutically acceptable enol ethers include, but are not limited to, derivatives of formula $C=C(OR)$ where R is hydrogen, alkyl, alkenyl, alkynyl, aryl, heteroaryl, aralkyl, heteroaralkyl, cycloalkyl [[ar]] and heterocyclyl. Pharmaceutically acceptable enol esters include, but are not limited to, derivatives of formula $C=C(OC(O)R)$ where R is hydrogen, alkyl, alkenyl, alkynyl, aryl, heteroaryl, aralkyl, heteroaralkyl, cycloalkyl [[ar]] and heterocyclyl. Pharmaceutically acceptable solvates and hydrates are complexes of a compound with one or more solvent or water molecules, or 1 to about 100, or 1 to about 10, or one to about 2, 3 or 4 solvent or water molecules.

Please replace the section on page 31, lines 1-6 with the following amended section:

R₁₂ and R₁₃ together form an optionally substituted 4-6 member ring and R₁₁[[,]] is selected from hydrogen, F, Cl, Br, CN, an optionally substituted C₁-C₄ alkyl, an optionally substituted C₂-C₄ alkenyl, an optionally substituted C₂-C₄ alkynyl, an optionally substituted C₁-C₄ haloalkyl, an optionally substituted C₁-C₄ heteroalkyl, -CONR₁₄R₁₅, an optionally substituted aryl, an optionally substituted heteroaryl, an optionally substituted heterocyclyl and an optionally substituted cycloalkyl;

Please replace the paragraph beginning on page 36, line 21 with the following amended paragraph:

In certain embodiments, R₂ is selected from hydrogen, fluoro, chloro, bromo, cyano, methyl, vinyl, hydroxymethyl, diethylaminomethyl, methoxymethoxymethyl, hydroxyiminomethyl, acetyloxymethyl, 1-hydroxy-2,2,2-trifluoroethyl, phenyl, trifluoromethoxy, trifluoromethylthio, acetyl, formyl, diethylaminocarbonyl, 3-formylphenyl, ~~N-benzyl-N-methylaminocarbonyl~~ N-benzyl-N-methylaminocarbonyl, dimethylaminocarbonyl, 1-pyrrolidinocarbonyl, 1-morpholinocarbonyl, 4-methylpiperazi-1-nocarbonyl, piperidinocarbonyl, N-cyclohexyl-N-methylaminocarbonyl, piperidinosulfonyl, and N,N-dimethylaminosulfonyl.

Please replace the paragraph beginning on page 36, line 29 with the following amended paragraph:

In certain embodiments, R₂ is selected from fluoro, chloro, bromo, cyano, methyl, vinyl, hydroxymethyl, diethylaminomethyl, methoxymethoxymethyl, hydroxyiminomethyl, acetyloxymethyl, 1-hydroxy-2,2,2-trifluoroethyl, phenyl, trifluoromethoxy, trifluoromethylthio, acetyl, formyl, diethylaminocarbonyl, 3-formylphenyl, ~~N-benzyl-N-methylaminocarbonyl~~ N-benzyl-N-methylaminocarbonyl, dimethylaminocarbonyl, 1-pyrrolidinocarbonyl, 1-morpholinocarbonyl, 4-methylpiperazi-1-nocarbonyl, piperidinocarbonyl, N-cyclohexyl-N-methylaminocarbonyl, piperidinosulfonyl, and N,N-dimethylaminosulfonyl.

Please replace the paragraph beginning on page 38, line 9 with the following amended paragraph:

In certain embodiments, R₃ is selected from fluoro, chloro, bromo, hydroxy, methoxy, methyl, tert-butyl, trifluoromethyl, hydroxymethyl, trifluoromethoxy, trifluoromethylthio, phenyl, 2,2-difluoro-1-ethoxy, ~~4,4,4-trifluoro~~ 4,4,4-trifluoro-but-1-oxy, 2,4-difluorophenyl, 2-fluorophenyl, phenoxy, 3,6-dichlorophenoxy, 4-methoxyphenoxy, 3,4-dichlorophenoxy, 4-methylphenoxy, 4-chlorophenoxy, 3-trifluoromethoxyphenoxy, 4-fluorophenoxy, 3-thienyl, 2,2-difluoro-3,3,3-trifluoroprop-1-yloxy, 3,5-dichlorophenoxy, 4-fluorobenzyloxy, 3-fluorobenzyloxy and 3-pyridyl.

Please replace the paragraphs on page 38, lines 23-30 with the following amended paragraphs:

In certain embodiments, R₄ is selected from hydrogen, halo, hydroxy, C₁-C₄ alkyl, C₂-C₄alkenyl, C₃-C₆cycloalkyl, haloC₁-C₄ alkyl, aryl, hydroxy C₁-C₄alkyl, alkoxy, haloalkoxy, aralkoxy, haloaralkoxy, alkylaralkoxy, haloaryl, or R₃ and R₄ together form ~~alkelenedioxy~~ alkylenedioxy.

In certain embodiments, R₄ is selected from halo, hydroxy, C₁-C₄ alkyl, C₂-C₄alkenyl, C₃-C₆cycloalkyl, haloC₁-C₄ alkyl, aryl, hydroxy C₁-C₄alkyl, alkoxy, haloalkoxy, aralkoxy, haloaralkoxy, alkylaralkoxy, haloaryl, or R₃ and R₄ together form ~~alkelenedioxy~~ alkylenedioxy.

Please replace the paragraphs on page 39, lines 6-14 with the following amended paragraphs:

In certain embodiments, R₄ is selected from hydrogen, chloro, bromo, hydroxy, methoxy, fluoro, trifluoromethoxy, methyl, ethyl, isopropyl, vinyl, benzyloxy, phenyl, cyclohexyl, trifluoromethyl, 4-methylbenzyloxy, hydroxymethyl, or R₃ and R₄ together form ~~an methelenedioxy~~ a methylenedioxy.

In certain embodiments, R₄ is selected from chloro, bromo, hydroxy, methoxy, fluoro, trifluoromethoxy, methyl, ethyl, isopropyl, vinyl, benzyloxy, phenyl, cyclohexyl, trifluoromethyl, 4-methylbenzyloxy, hydroxymethyl, or R₃ and R₄ together form ~~an methelenedioxy~~ a methylenedioxy.

Please replace the paragraph beginning on page 39, line 23 with the following amended paragraph:

In certain embodiments, R₂ and R₃ together form ~~alkelenedioxy~~ alkylenedioxy. In certain embodiments, R₂ and R₃ together with the phenyl ring on which they are substituted form optionally substituted benzo-1,3-dioxan or optionally substituted naphthyl ring.

Please replace the paragraph beginning on page 42, line 21 with the following amended paragraph:

In certain embodiments, at least one position selected from R₂, R₃, R₄, R₅, and R₆ is not hydrogen. ~~In certain embodiments, at least one position selected from R₇, R₈, R₉, and R₁₀ is not hydrogen.~~ In certain embodiments, if R₄ is F, then at least one position selected from R₂, R₃, R₅ and R₆ is not hydrogen. In certain embodiments, if R₃ is F, then at least one

position selected from R₂, R₄, R₅, and R₆ is not hydrogen. In certain embodiments, if any two positions selected from R₂, R₃, R₄, R₅, and R₆ are both F, then at least one of the other three positions selected from R₂, R₃, R₄, R₅, and R₆ is not hydrogen.

Please replace the text on page 44, line 5 with the following amended text:

In certain embodiments, at least one position selected from R₇, R₈, R₉, and R₁₀ is not hydrogen. In certain embodiments, R₁ is:

Please replace the paragraph beginning on page 45, line 3 with the following amended paragraph:

In certain embodiments, R₁₁ is selected from cyano, formyl, C₁-C₄alkyl, C₂-C₄alkenyl, C₂-C₄alkynyl, hydroxyC₁-C₄alkyl, haloC₁-C₄alkyl, haloC₂-C₄alkenyl, hydroxyC₁-C₄alkyl, hydroxyC₂-C₄alkenyl, cyanoC₁-C₄alkenyl, hydroxyC₂-C₄alkynyl, alkoxyalkoxyC₁-C₄alkyl, hydroxyhaloC₁-C₄alkyl, aminoC₁-C₄alkyl, C₁-C₄alkylaminoC₁-C₄alkyl, diC₁-C₄alkylaminoC₁-C₄alkyl, C₁-C₄alkylC₂-C₄alkenylaminoC₁-C₄alkyl, arylaminoC₁-C₄alkyl, C₂-C₄alkenylaminoC₁-C₄alkyl, cycloC₃-C₆alkylaminoC₁-C₄alkyl, hydroxyalkoxyalkyl, haloalkylcarbonyl, alkoxyalkoxyalkoxy, carboxyalkoxyalkyl, alkoxyhaloalkyl, alkoxyalkoxyalkenyl, hydroxy C₁-C₄alkylcarbonyl, N,N-diC₁-C₄alkylaminoC₁-C₄alkyl, N-cycloC₃-C₆alkyl-N-C₁-C₄alkylaminocarbonyl, haloC₁-C₄alkylcarbonyl, hydroxyhaloC₁-C₄alkyl, C₁-C₄alkylcarbonyl, cycloC₃-C₆alkylcarbonyl, C₂-C₄alkenylcarbonyl, C₂-C₄alkynylcarbonyl, arylcarbonyl, heteroarylcarbonyl, hydroxyaralkyl, C₁-C₄alkoxyC₁-C₄alkyl, C₂-C₄alkenylalkoxyC₁-C₄alkyl, C₂-C₄alkynylalkoxyC₁-C₄alkyl, aryloxyC₁-C₄alkyl, hydroxyiminoC₁-C₄alkyl, alkoxyiminoC₁-C₄alkyl, C₂-C₄alkenylalkoxyiminoC₁-C₄alkyl, aryloxyiminoC₁-C₄alkyl, aralkoxyiminoC₁-C₄alkyl, heterocyclyl, heteroaryl and ~~CONR₁₃R₁₄~~ -CONR₁₄R₁₅, wherein the alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, heteroaryl and aryl groups can be unsubstituted or substituted with one to three substituents selected from C₁-C₄-alkyl, C₂-C₄alkenyl, C₂-C₄alkynyl, hydroxy, C₁-C₄alkoxy, nitro, halo, cyano, oxo, aryl, cycloalkyl, heterocyclyl, and heteroaryl groups.

Please replace the paragraph beginning on page 46, line 8 with the following amended paragraph:

In certain embodiments, R₁₁ is selected from hydrogen, cyano, carbamoyl, hydroxymethyl, 1-hydroxyethyl, vinyl, acetyl, 1-hydroxy-1-methylethyl, methoxymethyl, 4-fluorophenylhydroxymethyl, cyclohexylhydroxymethyl, hydroxythien-3-ylmethyl,

hydroxythien-2-ylmethyl, N,N-diethylaminocarbonyl, methoxymethoxymethyl, 3-prop-2-enyloxymethyl, 1-hydroxybut-3-enyl, 1-hydroxy-2-phenylethyl, acroloyl, 4-fluorobenzoyl, thien-2-ylcarbonyl, cyclohexylcarbonyl, aminomethyl, phenylaminomethyl, prop-2-ynylaminomethyl, 2,2,2-[[,]]-trifluoroethylaminomethyl, cyclopropylaminomethyl, butylaminomethyl, 2-hydroxyethoxymethyl, isopropenyl, formyl, trifluoroacetyl, methoxyethoxymethoxy, 2,2,2-trifluoro-1-hydroxy-1-(trifluoromethyl)ethyl, but-2-ynloxymethyl, 1-cyanovinyl, prop-3-ynyloxymethyl, 4-hydroxybut-3-enyl, 1-hydroxy-2-trifluoroethyl, ethoxycarbonylmethoxymethyl, carboxymethoxymethyl, 1-hydroxyprop-2-ynyl, 1-methoxy-2,2,2-trifluoroethyl, 2,2,2-trifluoro-1-methoxy-1-(trifluoromethyl)ethyl, 1-hydroxy-1-(thien-3-yl)ethyl, 2-methoxycarbonylvinyl, hydroxyethylcarbamoyl, ethylcarbamoyl, 2-(carbomethoxy)pyrrolidinocarbonyl, piperazinocarbonyl, N,N-dimethylaminomethyl, N,N-dimethylaminocarbonyl, N-ethyl-N-methylaminocarbonyl, N-morpholinocarbonyl, cyclopropyl, N-cyclohexyl-N-methylaminocarbonyl, 1-pyrrolidinocarbonyl, 2,2,2-[[,]]-trifluoroethylcarbamoyl, 4-hydroxypiperidinecarbonyl, 4-methylpiperazinecarbonyl, 1-hydroxy-4,4,4-trifluorobut-2ynyl, 3-hydroxy-3-phenylpropanoyl, 3-hydroxy-3-butanoyl, N,N-dimethoxyethylaminocarbonyl, N-allyl-N-methylaminocarbonyl, 1-piperidinocarbonyl, 4-oxo-piperidin-1-ylcarbonyl, 4-(1,3-dioxan)piperidinopiperidino-carbonyl, piperidin-1-ylmethyl, benzoyl, 1-hydroxybenzyl, 1-hydroxyiminoethyl, 1-methoxyiminoethyl, 1-allyloxyiminoethyl, phenoxyiminoethyl, 1-ethoxyiminoethyl, 1-carboxymethoxyiminoethyl, 1-t-butyloxyiminoethyl, 1-benzyloxyiminoethyl, 1-(4-nitrobenzyl)oxyiminoethyl, 1-hydroxyiminomethyl, 1-hydroxyprop-2-ynyl, and but-2-enoyl.

Please replace the paragraph beginning on page 47, line 4 with the following amended paragraph:

In certain embodiments, R₁₁ is selected from hydroxymethyl, acetyl, 1-hydroxy-1-methylethyl, 1-hydroxyethyl, 1-hydroxyiminoethyl, 1-methoxyiminoethyl, 1-allyloxyiminoethyl, 1-phenoxyiminoethyl, 1-ethoxyiminoethyl, 1-tert-butoxyiminoethyl, 1-benzyloxyiminoethyl, hydroxyiminomethyl, methoxymethyl, methoxymethoxymethyl, 1-hydroxy-2,2,2-trifluoroethyl, cyclohexylcarbonyl, prop-2-ynylaminomethyl, ~~2,2,2-trifluoro~~ 2,2,2-trifluoroethylaminomethyl, 2-hydroxymethoxymethyl, 2-cyanovinyl, 1-methoxy-2,2,2-trifluoroethyl, ~~trifluoroethyl~~, 4-oxopiperidinocarbonyl, ~~2,2,2-trifluoro~~ 2,2,2-trifluoroethylcarbamoyl, pyrrolidinocarbonyl and piperidinocarbonyl.

Please replace the paragraph beginning on page 48, line 8 with the following amended paragraph:

In certain embodiments, R_{11} and R_{12} together form an optionally substituted 5-6 member ring and R_{13} is selected from hydrogen, F, Cl, Br, CN, $\text{CONR}_{14}\text{R}_{15}$, an optionally substituted $\text{C}_1\text{-C}_4$ alkyl, an optionally substituted $\text{C}_1\text{-C}_4$ haloalkyl, and an optionally substituted $\text{C}_1\text{-C}_4$ heteroalkyl. In certain embodiments, R_{12} and R_{13} together form an optionally substituted 4-6 member ring and $R_{11}[[,]]$ is selected from hydrogen, F, Cl, Br, CN, an optionally substituted $\text{C}_1\text{-C}_4$ alkyl, an optionally substituted $\text{C}_1\text{-C}_4$ haloalkyl, an optionally substituted $\text{C}_1\text{-C}_4$ heteroalkyl, $\text{-CONR}_{14}\text{R}_{15}$, and an optionally substituted aryl.

Please replace the entry on page 54 in row 2, column 1 of Table A with the following amended entry:

[[2]] R_2

Please replace the entry on page 54 in row 4, column 1 of Table A with the following amended entry:

[[3]] R_3

Please replace the entry on page 54 in row 7, column 1 of Table A with the following amended entry:

[[4]] R_4

Please replace the entry on page 55 in row 2, column 1 of Table A with the following amended entry:

[[5]] R_5

Please replace the entry on page 55 in row 3, column 1 of Table A with the following amended entry:

[[6]] R_6

Please replace the entry on page 55 in row 4, column 1 of Table A with the following amended entry:

[[7]] R_7

Please replace the entry on page 55 in row 6, column 1 of Table A with the following amended entry:

[[8]] R₈

Please replace the entry on page 56 in row 1, column 1 of Table A with the following amended entry:

[[9]] R₉

Please replace the entry on page 56 in row 3, column 1 of Table A with the following amended entry:

[[10]] R₁₀

Please replace the entry on page 56 in row 4, column 1 of Table A with the following amended entry:

[[11]] R₁₁

Please replace the entry on page 56 in row 6, column 1 of Table A with the following amended entry:

[[12]] R₁₂

Please replace the entry on page 57 in row 2, column 1 of Table A with the following amended entry:

[[13]] R₁₃

Please replace the entry on page 57 in row 4, column 1 of Table A with the following amended entry:

[[14]] R₁₄

Please replace the entry on page 57 in row 6, column 1 of Table A with the following amended entry:

[[15]] R₁₅

Please replace the entry on page 57 in row 8, column 1 of Table A with the following amended entry:

[[16]] R₁₆

Please replace the entry on page 58 in row 1, column 1 of Table A with the following amended entry:

[[17]] R₁₇

Please replace the section on page 59, lines 19-20 with the following amended section:

(Z)-5-(3',5'-di(~~trifluoromethyl~~)(trifluoromethyl)benzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (compound 32);

Please replace the section on page 59, lines 27-28 with the following amended section:

(Z)-5-(4'-ethylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (compound [[38]] 36);

Please replace the section on page 60, lines 1-2 with the following amended section:

(Z)-5-(2'-chloro-6'-fluorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (compound [[36]] 38);

Please replace the section on page 60, lines 9-10 with the following amended section:

(Z)-5-(2'-(6'-methyl-pyridinyl~~methylidene~~methylidene))-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (compound 42);

Please replace the section on page 61, lines 23-24 with the following amended section:

(Z)-5-(3',4'-methylenedioxybenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]~~quinoline (compound 67)~~quinoline (compound 67);

Please replace the section on page 62, lines 15-16 with the following amended section:

(Z)-5-(2'-(3''-~~benzenecarbaldehyde-formyl~~phenyl)benzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (compound 79);

Please replace the section on page 63, lines 1-3 with the following amended section:

(Z)-5-(2'-(dimethylamino)carbonyl-5'-bromo-~~fluore~~benzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (compound 85);

Please replace the section on page 63, lines 29-31 with the following amended section:

(Z)-5-(2'-(~~morpholinemorpholinocarbonyl~~)-4'-fluorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (compound 96);

Please replace the section on page 64, lines 1-3 with the following amended section:

(Z)-5-(8'-(6'-fluoro-benzo-1',3'-dioxan-~~methyldiene~~methyldiene))-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (compound 97);

Please replace the section on page 65, lines 6-11 with the following amended section:

(Z)-5-(1'-~~naphthyl~~1'-naphthylmethyldiene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (compound 111);

(Z)-5-(3'-methyl-4'-methoxybenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-~~2,2-cyclohexyl-4-~~2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (compound 112);

(Z)-5-(2',5'-dimethoxybenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-~~2,2-cyclohexyl-4-~~2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (compound 113);

Please replace the section on page 65, lines 24-26 with the following amended section:

(Z)-5-(8'-(6'-chloro-benzo-1',3'-dioxan-~~methyldiene~~methyldiene))-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (compound 120);

Please replace the section on page 66, lines 1-3 with the following amended section:

(Z)-5-(8'-(6'-methyl-benzo-1',3'-dioxan-~~methyldiene~~methyldiene))-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (compound 123);

Please replace the section on page 66, lines 6-10 with the following amended section:

(Z)-5-(8'-(5',6'-difluoro-benzo-1',3'-dioxan-~~methyldienemethylidene~~))-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (compound 125);
(Z)-5-(3'-(3'',5''-~~dichloro~~-dichlorophenoxy)benzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (compound 126);

Please replace the section on page 68, lines 13-15 with the following amended section:

(Z)-5-(2'-(5'-Methyl-3'-(~~piperidine~~piperidinecarbonyl)furanylmethylidene))1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno(3,4-f)quinoline (compound 151);

Please replace the section on page 72, lines 4-5 with the following amended section:

(Z)-5-((E)-2'-(Hydroxyiminomethyl)benzylidene)1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno(3,4-f)quinoline (compound 192);

Please replace the section on page 72, lines 11-13 with the following amended section:

(Z)-5-(2'-(3'-(~~Prop-Prop~~-2''-enyloxymethylmethyl)thienylmethylidene))1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno(3,4-f)quinoline (compound 195);

Please replace the section on page 74, lines 9-11 with the following amended section:

(Z)-5-(2'-([3'']3'-(Thien-3''-ylcarbonyl)thienylmethylidene))1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno(3,4-f)quinoline (compound 215);

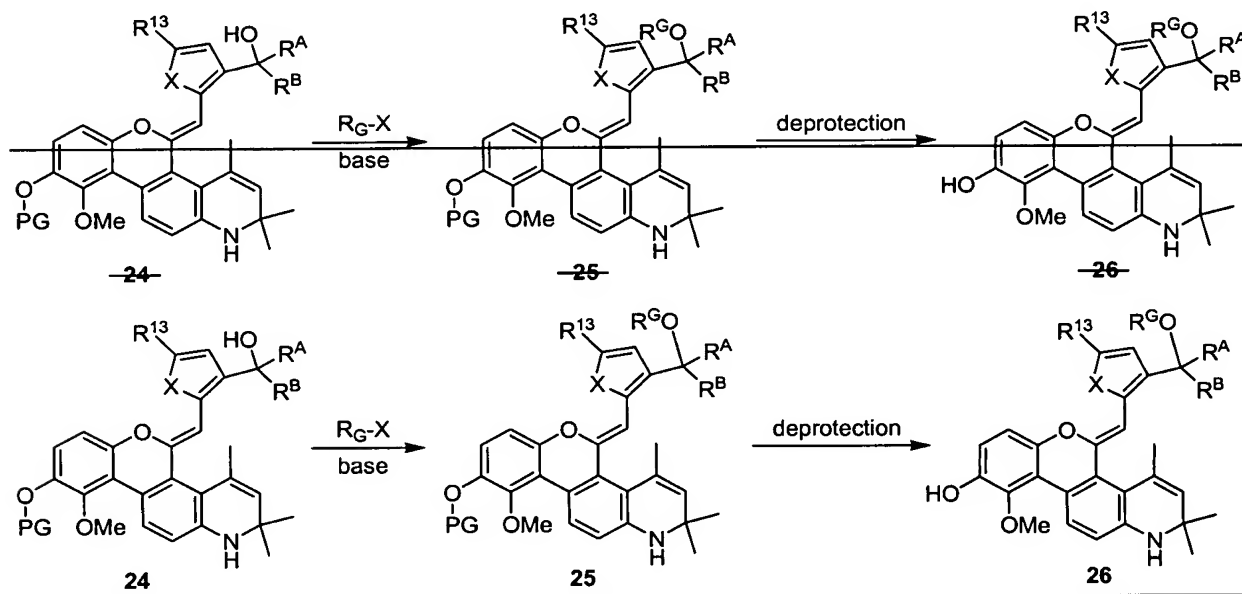
Please replace the section on page 76, lines 25-27 with the following amended section:

(Z)-5-(2'-(3'-(1''-Hydroxy-1''-(thien-[[3'']]3'''-yl)ethyl)thienylmethylidene))1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno(3,4-f)quinoline (compound 245);

Please replace the section on page 78, lines 1-3 with the following amended section:

(Z)-5-(2'-(3''-(3'''3'-(3''-Hydroxybutanoyl)thienylmethylidene))1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno(3,4-f)quinoline (comopund 259); and

Please replace Scheme VII on page 83, lines 25-35 with the following amended scheme:



Please replace the paragraph beginning on page 94, line 12 with the following amended paragraph:

The compositions are intended to be administered by a suitable route, including orally in the form of capsules, tablets, granules, powders or liquid formulations including syrups; parenterally, such as subcutaneously, intravenously, ~~intramiscularly~~ intramuscularly, with ~~inteasternal~~ intersternal injection or infusion techniques (as sterile injectable aq. or non-aq. solutions or suspensions); nasally such as by inhalation spray; topically, such as in the form of a cream or ointment; rectally such as in the form of suppositories; liposomally; and locally. The compositions can be in liquid, semi-liquid or solid form and are formulated in a manner suitable for each route of administration. In certain embodiments, administration of the formulation include parenteral and oral modes of administration. In one embodiment, the compositions are administered orally.

Please replace the paragraph beginning on page 100, line 4 with the following amended paragraph:

In certain embodiments, a pharmaceutical composition containing one or more compounds provided herein is useful for treating a condition[[s]] or disorder in a mammalian, and particularly in a human patient. Suitable administration routes include, but are not limited to, oral, rectal, transmucosal, intestinal, enteral, topical, suppository, through inhalation, intrathecal, intraventricular, intraperitoneal, intranasal, intraocular and parenteral (e.g., intravenous, intramuscular, intramedullary, and subcutaneous). In certain embodiments, pharmaceutical compositions are administered to achieve local rather than systemic exposures. For example, pharmaceutical compositions may be injected directly in the area of desired effect (e.g., in the renal or cardiac area). In certain embodiments in which the pharmaceutical composition is administered locally, the dosage regimen is adjusted to achieve a desired local concentration of a compound provided herein.

Please replace the paragraph beginning on page 105, line 29 with the following amended paragraph:

For a solid dosage form, the solution or suspension, in for example propylene carbonate, vegetable oils or triglycerides, is preferably encapsulated in a gelatin capsule. Such solutions, and the preparation and encapsulation thereof, are disclosed in U.S. Patent [[Nos]] Nos. 4,328,245; 4,409,239; and 4,410,545. For a liquid dosage form, the solution, [[e.g.,]] for example, in a polyethylene glycol, can be diluted with a sufficient quantity of a pharmaceutically acceptable liquid carrier, *e.g.*, water, to be easily measured for administration.

Please replace the paragraph beginning on page 106, line 27 with the following amended paragraph:

In all embodiments, tablet[[s]] and capsule[[s]] formulations can be coated as known by those of skill in the art in order to modify or sustain dissolution of the active ingredient. Thus, for example, they can be coated with a conventional enterically digestible coating, such as phenylsalicylate, waxes and cellulose acetate phthalate.

Please replace the paragraph beginning on page 112, line 27 with the following amended paragraph:

Topical mixtures are prepared as described for [[the]] local and systemic administration. The resulting mixture can be a solution, suspension, emulsion[[s]] or the like

and are formulated as creams, gels, ointments, emulsions, solutions, elixirs, lotions, suspensions, tinctures, pastes, foams, aerosols, irrigations, sprays, suppositories, bandages, dermal patches or any other formulations suitable for topical administration.

Please replace the paragraph beginning on page 114, line 24 with the following amended paragraph:

In certain embodiments, the pharmaceutical composition is prepared for topical administration such as rectal administration. The pharmaceutical dosage forms for rectal administration include, but are not limited to rectal suppositories, capsules and tablets for systemic effect. Rectal suppositories ~~[[are]]~~ as used herein mean solid bodies for insertion into the rectum which melt or soften at body temperature releasing one or more pharmacologically or therapeutically active ingredients. Pharmaceutically acceptable substances utilized in rectal suppositories are bases or vehicles and agents to raise the melting point. Examples of bases include cocoa butter (theobroma oil), glycerin-gelatin, carbowax (polyoxyethylene glycol) and appropriate mixtures of mono-, di- and triglycerides of fatty acids. Combinations of the various bases can be used. In certain embodiments, the pharmaceutical compositions contain bland moisturizing bases, such as ointments or creams. Exemplary suitable ointment bases include, but are not limited to, petrolatum, petrolatum plus volatile silicones, lanolin and water in oil emulsions such as Eucerin™, available from Beiersdorf (Cincinnati, Ohio). Exemplary suitable cream bases include, but are not limited to, Nivea™ Cream, available from Beiersdorf (Cincinnati, Ohio), cold cream (USP), Purpose Cream™, available from Johnson & Johnson (New Brunswick, New Jersey), hydrophilic ointment (USP) and Lubriderm™, available from Pfizer (Morris Plains, New Jersey). Agents to raise the melting point of suppositories include spermaceti and wax. Rectal suppositories can be prepared either by the compressed method or by molding. The typical weight of a rectal suppository is about 2 to 3 ~~[[gm]]~~ grams.

Please replace the paragraph beginning on page 115, line 19 with the following amended paragraph:

The compounds or pharmaceutically acceptable derivatives can be packaged as articles of manufacture containing packaging material, within the ~~packaing~~ packaging material a compound or pharmaceutically acceptable derivative thereof provided herein, which is effective for modulating the activity of glucocorticoid receptor, or for treatment,

prevention or amelioration of one or more symptoms of glucocorticoid receptor mediated diseases or disorders, or diseases or disorders in which glucocorticoid receptor activity is implicated, and a label that indicates that the compound or composition, or pharmaceutically acceptable derivative thereof, is used for modulating the activity of glucocorticoid receptor or for treatment, prevention or amelioration of one or more symptoms of glucocorticoid receptor mediated diseases or disorders, or diseases or disorders in which glucocorticoid receptor activity is implicated.

Please replace the paragraph beginning on page 116, line 11 with the following amended paragraph:

In certain embodiments, the pharmaceutical compositions can be presented in a pack or dispenser device which can contain one or more unit dosage forms containing a compound provided herein. The pack can for example contain metal or plastic foil, such as a blister pack. The pack or dispenser device can be accompanied by instructions for administration. The pack or dispenser can also be accompanied with a notice associated with the container in a form prescribed by a governmental agency regulating the manufacture, use, or sale of pharmaceuticals, which notice is reflective of approval by the agency of the form of the drug for human or veterinary administration. Such notice, for example, can be the labeling approved by the U.S. Food and Drug Administration for prescription drugs, or the approved product insert. Compositions containing a compound provided herein formulated in a compatible pharmaceutical carrier can also be prepared, placed in an appropriate container, and labeled for treatment of an indicated condition.

Please replace the paragraph beginning on page 116, line 25 with the following amended paragraph:

Standard physiological, pharmacological and biochemical procedures are available for testing the compounds provided herein to identify those that possess activity as glucocorticoid receptor modulators. In vitro and in vivo assays known in the art can be used to evaluate the activity of the compounds provided herein as glucocorticoid receptor modulators. Exemplary assays include, but are not limited to fluorescence polarization assay, luciferase assay, ~~co-transfection~~ and co-transfection assay. In certain embodiments, the compounds provided herein are capable of modulating activity of glucocorticoid receptor in a "co-transfection" assay (also called a "cis-trans" assay), which is known in the art. *See e.g.,*

Evans *et al.*, *Science*, 240:889-95 (1988); U.S. Patent Nos. 4,981,784 and 5,071,773; Pathirana *et al.*, "Nonsteroidal Human Progesterone Receptor Modulators from the Marie Alga *Cymopolia Barbata*," *Mol. Pharm.* 47:630-35 (1995)). Modulating activity in a co-transfection assay has been shown to correlate with *in vivo* modulating activity. Thus, in certain embodiments, such assays are predictive of *in vivo* activity. See, e.g., Berger *et al.*, *J. Steroid Biochem. Molec. Biol.* 41:773 (1992).

Please replace the paragraph beginning on page 118, line 11 with the following amended paragraph:

Methods of use of the compounds and compositions provided herein also are provided. The methods include *in vitro* and *in vivo* uses of the compounds and compositions for altering glucocorticoid receptor activity and for treatment, prevention, or amelioration of one or more symptoms of diseases or ~~disorder~~ disorders that are modulated by glucocorticoid receptor activity, or in which glucocorticoid receptor activity[[,]] is implicated. In certain embodiments, provided herein are methods of treating a ~~patient~~ patient by administering a compound provided herein. In certain embodiments, such patient exhibits symptoms or signs of a glucocorticoid receptor mediated condition.

Please replace the paragraph beginning on page 119, line 26 with the following amended paragraph:

In certain embodiments, one or more compounds provided herein are co-administered with one or more other pharmaceutical agents or treatments. In certain embodiments, such one or more other pharmaceutical agents are designed to treat the same disease or condition as the compounds provided herein. In certain embodiments, such one or more other pharmaceutical agents are designed to treat a different disease or condition as the compounds provided herein. In certain embodiments, such one or more other pharmaceutical agents are designed to treat an undesired effect of the compounds provided herein. In certain embodiments, the compounds provided herein [[is]] are co-administered with another pharmaceutical agent to treat an undesired effect of that other pharmaceutical composition. In certain embodiments, the compounds provided herein and one or more other pharmaceutical agents are administered at the same time. In certain embodiments, the compounds provided herein and one or more other pharmaceutical agents are administered at different times. In certain embodiments, the compounds provided herein and one or more

other pharmaceutical agents are prepared together in a single formulation. In certain embodiments, the compounds provided herein and one or more other pharmaceutical agents are prepared separately.

Please replace the section on page 137, lines 3-5 with the following amended section:

(Z)-5-(2'-(6'-methyl-pyridinyl)methylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 42, structure 1 of Scheme I, where R¹ = (2-(6-methylpyridinyl))

Please replace the paragraph beginning on page 154, line 8 with the following amended paragraph:

This compound was prepared according to General Method 1 (Example 1) from Compound 21 and 3-carbaldehydephenylboronic acid. ¹H NMR (500 MHz, CDCl₃) δ 9.98 (s, 1H), 8.25 (d, J = 8.5 Hz, 1H), 7.87 (m, 1H), 7.77 (m, 1H), 7.55 (m, 2H), 7.48 (m, 1H), 7.29 (m, 1H), 7.25 (m, 1H), 6.82 (d, J = 8.5 Hz, 1H), 6.73 (d, J = 8.9 Hz, [1H]), 6.67 (d, J = 8.9 Hz, 1H), 5.51 (s, 1H), 5.17 (d, J = 1.2 Hz, 1H), 3.81 (s, 3H), 1.91 (s, 3H), 1.29 (br s, 6H).

Please replace the paragraph beginning on page 157, line 14 with the following amended paragraph:

This compound was prepared according to General Method 2 (Example 60) from 5-bromo-2-(dimethylaminocarbonyl)toluene. ¹H NMR (500 MHz, CD₃OD) δ 8.63 (d, J = 1.8 Hz, 1H), 8.34 (d, J = 8.9 Hz, 1H), 7.42 (dd, J = 8.1, 2.0 Hz, 1H), 7.11 (d, J = 8.2 Hz, 1H), 6.79-6.75 (m, 3H), 5.51 (d, J = 1.2 Hz, 1H), 5.49 (s, 1H), 3.77 (s, 3H), 3.03 (s, 3H), 2.79 (br s, 3H), 2.03 (d, J = 1.2 Hz, 3H), 1.29 (br s, 6H).

Please replace the paragraphs on page 163, lines 6-15 with the following amended paragraphs:

(Z)-5-(2'-(morpholinomorpholinocarbonyl)-4'-fluorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 96, structure 1 of Scheme I, where R¹ = 4-fluoro-2-(morpholinomorpholinocarbonyl)phenyl)

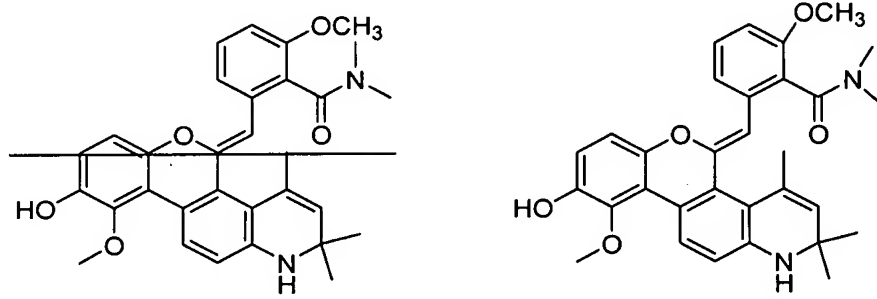
This compound was prepared according to General Method 2 (Example 60) from 4-fluoro-2-(morpholinomorpholinocarbonyl)toluene. ¹H NMR (500 MHz, CD₃OD) δ 8.40-8.38 (m, 1H), 8.30 (d, J = 8.5 Hz, 1H), 7.25 (ddd, J = 11.4, 8.7, 2.7 Hz, 1H), 7.03 (dd, J = 8.5, 3.1

Hz, 1H), 6.79-6.74 (m, 1H), 6.71 (d, $J = 8.9$ Hz, 1H), 5.55 (1H, s), 5.50 (d, $J = 1.2$ Hz, 1H), 3.74 (s, 3H), 3.67-3.65 (m, 2H), 3.59-3.56 (m, 2H), 3.46-3.44 (m, 1H), 3.23-3.21 (m, 1H), 3.11-3.09 (m, 1H), 2.05 (d, $J = 1.2$ Hz, 3H), 1.32 (s, 3H), 1.28 (s, 3H).

Please replace the section on page 163, lines 18-20 with the following amended section:

(Z)-5-(8'-(6'-fluoro-benzo-1',3'-dioxan-~~methylidene~~methylidene))-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 97, structure 1 of Scheme I, where $R^1 = 8$ -(6-fluoro-benzo-1,3-dioxan))

Please replace the structure on page 164, line 8 with the following amended structure:



Please replace the paragraph beginning on page 165, line 3 with the following amended paragraph:

This compound was prepared according to General Method 2 (Example 60) from 4-fluoro-2-(4'-methylpiperazinecarbonyl)toluene. ^1H NMR (500 MHz, CD_3OD) δ 8.40-8.38 (m, 1H), 8.31 (d, $J = 8.9$ Hz, 1H), 7.25 (ddd, $J = 11.6, 8.9, 2.9$ Hz, 1H), 7.02 (dd, $J = 8.5, 2.7$ Hz, 1H), 6.76 (d, $J = 8.9, 3.1$ Hz, 1H), 6.70 (d, $J = 8.7$ Hz, 1H), 5.51 (s, 1H), 5.50 (m, [[1H]]) 1H, 3.75 (s, 3H), 3.63-3.61 (m, 1H), 3.30 (m, 2H, obscured by solvent), 3.15-3.05 (m, 2H), 2.43-2.41 (m, 2H), 2.21-2.19 (m, 4H), 2.04 (d, $J = 1.5$ Hz, 3H), 1.31-1.28 (m, 6H).

Please replace the paragraph beginning on page 166, line 14 with the following amended paragraph:

This compound was prepared according to General Method 2 (Example 60) from 4-fluoro-2-(piperidinecarbonyl)toluene. ^1H NMR (500 MHz, CD_3OD) δ 8.41-8.39 (m, 1H), 8.29 (d, $J = 8.5$ Hz, 1H), 7.25 (ddd, $J = 11.6, 8.7, 2.7$ Hz, 1H), 6.97 (dd, $J = 8.5, 2.7$ Hz, 1H), 6.75 (d, $J = 8.9$ Hz, 1H), 6.69 (d, $J = 8.5$ Hz, 1H), 5.52 (1H, s), 5.47 (d, $J = 0.6$ Hz, 1H), 3.73

(s, 3H), 3.69-3.67 (m, 1H), 3.53-3.52 (m, 1H), 3.14-3.08 (m, 2H), 2.04 (s, 3H), 1.57-1.54 (m, [[4H]]) 4H), 1.30-1.28 (m, 8H).

Please replace the paragraphs on page 172, lines 5-12 with the following amended paragraphs:

(Z)-5-(3'-methyl-4'-methoxybenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-~~2,2-cyclohexyl-4~~-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 112, structure 1 of Scheme I, where R¹ = 4-methoxy-3-methylphenyl)

This compound was prepared according to General Method 1 (Example 1) from 4-methoxy-3-methylbenzyl bromide. ¹H NMR (500 MHz, CDCl₃) δ 8.13 (d, J = 8.6 Hz, 1H), 7.63 (m, 1H), 7.54 (~~(m, 1H)~~), (m, 1H), 6.89 (d, J = 7.9 Hz, 1H), 6.83 (d, J = 8.6 Hz, 1H), 6.66 (d, J = 8.6 Hz, 1H), 6.14 (s, 1H), 5.56 (s, 1H), 5.50 (m, 2H), 4.16 (s, 1H), 3.85 (s, 3H), 3.81 (s, 3H), 2.25 (s, 3H), 2.09 (s, 3H), 1.35 (br s, 6H).

Please replace the section on page 172, lines 15-17 with the following amended section:

(Z)-5-(2',5'-dimethoxybenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-~~2,2-4~~-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 113, structure 1 of Scheme I, where R¹ = 2,5-dimethoxyphenyl)

Please replace the section on page 176, lines 3-5 with the following amended section:

(Z)-5-(8'-(6'-chloro-benzo-1',3'-dioxan-~~methylidene~~methylidene))-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 120, structure 1 of Scheme I, where R¹ = 8-(6-chloro-benzo-1,3-dioxan))

Please replace the section on page 177, lines 12-14 with the following amended section:

~~(Z)-5-(8'-(Z)-5-(8'-(6'-methyl-benzo-1',3'-dioxan-~~methylidene~~methylidene)))~~-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 123, structure 1 of Scheme I, where R¹ = 8-(6-methyl-benzo-1,3-dioxan))

Please replace the section on page 178, lines 12-14 with the following amended section:

(Z)-5-(8'-(5',6'-difluoro-benzo-1',3'-dioxan-~~methylidene~~methylidene))-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 125, structure 1 of Scheme I, where R¹ = 8-(5,6-difluoro-benzo-1,3-dioxan))

Please replace the section on page 179, lines 3-5 with the following amended section:

(Z)-5-(3'-(3'',5''-~~dichloro~~dichlorophenoxy)benzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 126, structure 1 of Scheme I, where R¹ = 3-(3',5'-dichlorophenoxy)phenyl)

Please replace the paragraph beginning on page 180, line 8 with the following amended paragraph:

This compound was prepared according to General Method 1 (Example 1) from 3-(3',4'-dichlorophenoxy)benzyl bromide. ¹H NMR (400 MHz, CDCl₃) δ 8.15 (d, *J* = 8.6 Hz, 1H), 7.57 (s, 1H), 7.43-7.39 (m, 2H), 7.33 (t, *J* = 7.9 Hz, 1H), 7.16 (d, *J* = 2.7 Hz, 1H), 6.93 (dd, *J* = 8.8, 2.8 Hz, 1H), 6.89 (d, *J* = 7.8 Hz, 1H), 6.80 (d, *J* = 8.8 Hz, 1H), 6.67 (d, *J* = 8.6 Hz, 1H), 6.56 (d, *J* = 8.7 Hz, [[1H]]) 1H, 5.58 (s, 1H), 5.56 (s, 1H), 5.51 (s, 1H), 4.19 (s, 1H), 3.77 (s, 3H), 2.08 (s, 3H), 1.35 (br s, 6H).

Please replace the paragraph beginning on page 183, line 13 with the following amended paragraph:

This compound was prepared according to General Method 2 (Example 60) from 2-methyl-3-(~~morpholine~~morpholinocarbonyl)thiophene. ¹H NMR (500 MHz, CD₃OD) δ 8.34 (d, *J* = 8.8 Hz, 1H), 7.41 (d, *J* = 5.4 Hz, 1H), 7.00 (dd, *J* = 5.4, 1H), 6.95 (d, *J* = 8.8 Hz, 1H), 6.77 (d, *J* = 8.3 Hz, 1H), 6.75 (d, *J* = 8.8 Hz, 1H), 5.95 (s, 1H), 5.51 (d, *J* = 1.5 Hz, 1H), 3.76 (s, 3H), 3.70-3.68 (m, 3H), 3.52-3.50 (m, 3H), 3.34-3.30 (m, 2H, partially obscured by solvent), 2.02 (d, *J* = 1.0 Hz, 3H), 1.30 (br s, 6H).

Please replace the paragraph beginning on page 189, line 12 with the following amended paragraph:

This compound was prepared according to General Method 2 (Example 60) from 2-methyl-5-(~~morpholine~~morpholinocarbonyl)thiophene. ¹H NMR (500 MHz, CD₃OD) δ 8.31

(d, $J = 8.8$ Hz, 1H), 7.27 (d, $J = 3.9$ Hz, 1H), 6.98 (d, $J = 3.9$ Hz, 1H), 6.95 (d, $J = 8.8$ Hz, 1H), 6.73 (d, $J = 8.3$ Hz, 1H), 6.71 (d, $J = 8.8$ Hz, 1H), 5.91 (s, 1H), 5.48 (d, $J = 1.5$ Hz, 1H), 3.78-3.76 (m, 4H), 3.73 (s, 3H), 3.71-3.69 (m, 4H), 1.99 (d, $J = 1.0$ Hz, 3H), 1.27 (m, 6H).

Please replace the section on page 204, lines 16-18 with the following amended section:

(Z)-5-(2'-(3'-(Dimethylaminomethyl)thienylmethylidene))1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 166, Structure 10 of Scheme III, where X = S, $R^{13} = H$, $R^{19}, R^{20}, R^{14}, R^{15} = Me$).

Please replace the paragraph beginning on page 208, line 18 with the following amended paragraph:

This compound was prepared according to General Method 9 (EXAMPLE 155) from Compound 170 (EXAMPLE 154) to afford Compound 172. 1H NMR (500MHz, $CDCl_3$) δ 8.16 (d, $J = 8.5$ Hz, 1H), 7.36 (d, $J = 7.5$ Hz, 2H), 7.31 (t, $J = 7.5$ Hz, 2H), 7.27 (m, 1H), 7.23 (d, $J = 5.4$ Hz, 1H), 7.07 (d, $J = 5.4$ Hz, 1H), 7.04 (d, $J = 8.8$ Hz, 1H), 6.83 (d, $J = 8.8$ Hz, 1H), 6.66 (d, $J = 8.5$ Hz, 1H), 6.13 (s, 1H), 5.99 (q, $J = 1.5$ Hz, 1H), 5.57 (s, 1H), 5.47 (s, 1H), 4.19 (s, 1H), 3.76 (s, 3H), 2.14 (br, 1H), 1.89 (m, 3H), 1.36 (~~(s, 6H)~~) ((s, 6H)).

Please replace the paragraph beginning on page 216, line 24 with the following amended paragraph:

(Z)-5-(2'-(3'-(Piperidinecarbonyl)thienylmethylidene))-1,2-dihydro-10-methoxy-2,2,4-trimethyl-9-(triisopropylsilyl)oxy-5H-chromeno[3,4-f]quinoline (Structure 12 of Scheme IV, where X = S, PG = triisopropylsilyl, $R^{13} = H$, $R^{14}R^{15} = \text{---}(\text{CH}_2)_5\text{---}$ (~~$\text{---}(\text{CH}_2)_5\text{---}$~~)). This compound was prepared according to General Method 3 (EXAMPLE 135) from Compound 140 (EXAMPLE 124) to afford (Z)-5-(2'-(3'-(Piperidinecarbonyl)thienylmethylidene))-1,2-dihydro-10-methoxy-2,2,4-trimethyl-9-(triisopropylsilyl)oxy-5H-chromeno[3,4-f]quinoline.

Please replace the paragraph beginning on page 218, line 17 with the following amended paragraph:

(Z)-5-(2'-(3'-((E)-Hydroxyiminomethyl)thienylmethylidene))1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 190, Structure 22 of Scheme V, where X = S, $R^{13} = H$, $R^A = Me$, $R^C = (E)\text{---}OH$). This compound was prepared

according to General Method 12 (EXAMPLE 167) from (Z)-5-(2'-(3'-((E)-hydroxyiminomethyl)thienylmethylidene))-1,2-dihydro-10-methoxy-2,2,4-trimethyl-9-(triisopropylsilyl)oxy-5H-chromeno[3,4-f]quinoline to afford Compound 190. ¹H NMR (500 MHz, Acetone-d₆) δ 10.19 (s, 1H), 8.33 (d, J=8.6 Hz, 1H), 8.24 (s, 1H), 7.82 (s, 1H), 7.40 (dd, J=5.3, 0.6 Hz, 1H), 7.30 (d, J=5.3 Hz, 1H), 7.01 (d, J=8.6 Hz, 1H), 6.83 (d, J=8.6 Hz, 1H), 6.82 (d, J=8.6 Hz, 1H), 6.39 (d, J=0.6 Hz, 1H), 5.94 (s, 1H), 5.58 (q, J=1.4 Hz, 1H), 3.78 (s, 3H), 2.06 (d, J=1.4 Hz, 3H), 1.35 (s, 6H).

Please replace the section on page 221, lines 25-29 with the following amended section:

¹H NMR (500MHz, ~~CDCl₃~~ CDCl₃) δ 8.35 (s, 1H), 8.18 (d, J=8.5 Hz, 1H), 8.06 (dd, J=7.7, 1.0 Hz, 1H), 7.70 (dd, J=7.7, 1.0 Hz, 1H), 7.42 (td, J=7.7, 1.0 Hz, 1H), 7.24 (td, J=7.7, 1.0 Hz, 1H), 7.18 (s, 1H), 6.78 (d, J=8.8 Hz, 1H), 6.75 (d, J=8.8 Hz, 1H), 6.70 (d, J=8.5 Hz, 1H), 5.99 (s, 1H), 5.57 (s, 1H), 5.53 (m, 1H), 4.21 (s, 1H), 3.80 (s, 3H), 2.14 (d, J=1.2 Hz, 3H), 1.36 (s, 6H).

Please replace the paragraph beginning on page 222, line 6 with the following amended paragraph:

General Method 13: Alkylation of an alcohol with an alkyl halide and a base. A solution of the alcohol (1 equiv.), base (10 equiv.) in THF (0.02 to 0.1 M) at 0 °C. The reaction suspension was allowed to warm to room temperature, stirred for 0.5 h and re-cooled to 0 °C before the addition of the alkyl halide (10 equiv.). The reaction was allowed to warm to room temperature and stirred for 4 h, a saturated solution of ammonium chloride (50 mL/mmol) was added, ethyl acetate (50 mL/mmol) was added and the layers separated. The aqueous layer was extracted with ethyl acetate (3 × 25 mL/mmol), the combined organic extracts were washed with a saturated solution of ammonium chloride (200 mL/mmol), dried (Na₂SO₄) and concentrated under reduced pressure. Purification by flash chromatography, eluting with ethyl acetate:hexanes, afforded the desired alcohol as a yellow oil. In certain instances, less base can be required.

Please replace the section on page 223, lines 12-15 with the following amended section:

(Z)-5-(2'-(3'-(Methoxymethoxymethyl)thienylmethylidene))1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline ~~[[carraige return]]~~ (Compound Compound 194, Structure 15 of Scheme IV, where X = S, R¹³ = H, R^D = methoxymethyl).

Please replace the paragraph beginning on page 223, line 25 with the following amended paragraph:

(Z)-5-(2'-(3'-(Methoxymethoxymethyl)thienylmethylidene))1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 194, Structure 15 of Scheme IV, where X = S, ~~[[R13]]~~ R¹³ = H, ~~[[RD]]~~ R^D = methoxymethyl). This compound was prepared according to General Method 12 (EXAMPLE 167) from (Z)-5-(2'-(3'-(methoxymethoxymethyl)thienylmethylidene))1,2-dihydro-10-methoxy-2,2,4-trimethyl-9-(triisopropylsilyl)oxy-5H-chromeno[3,4-f]quinoline to afford Compound 194. ¹H NMR (500 MHz, ~~Aeetone~~ Acetone-d₆) δ 8.31 (d, J=8.6 Hz, 1H), 7.78 (s, 1H), 7.35 (dd, J=5.2, 0.6 Hz, 1H), 7.04 (d, J=5.2 Hz, 1H), 7.00 (d, J=8.6 Hz, 1H), 6.81 (d, J=8.6 Hz, 1H), 6.80 (d, J=8.6 Hz, 1H), 6.21 (d, J=0.6 Hz, 1H), 5.90 (s, 1H), 5.54 (q, J=1.3 Hz, 1H), 4.62 (s, 2H), 4.56 (s, 2H), 3.77 (s, 3H), 3.32 (s, 3H), 2.07 (d, J=1.3 Hz, 3H), 1.34 (s, 6H).

Please replace the paragraph beginning on page 228, line 23 with the following amended paragraph:

General Method 15. Addition of a trifluoromethyl group generated from ~~(trifluoromethyl)~~ trifluoromethyltrimethylsilane and a fluoride source. Trifluoromethyltrimethylsilane (10 equiv₂) was added to a solution of the carbonyl compound (1 equiv₂) in THF (0.01-0.1 M). The solution was cooled to 0 °C before the dropwise addition of 1M tetrabutylammonium fluoride in THF (5 equiv₂) over 0.2 h. The reaction solution was stirred for an additional 0.2 h, a saturated solution of ammonium chloride (75 mL/mmol) was added, ethyl acetate (75 mL/mmol) was added and the layers separated. The aqueous layer was extracted with ethyl acetate (3 × 40 mL/mmol), the combined organic extracts washed with a saturated solution of ammonium chloride (100 mL/mmol), dried (Na₂SO₄) and concentrated under reduced pressure. Purification by flash chromatography, eluting with ethyl acetate:hexanes afforded the desired alcohol as a yellow oil.

Please replace the paragraph beginning on page 229, line 10 with the following amended paragraph:

(Z)-5-(2'-(3'-Piperidinecarbonylthienylmethylidene))1,2-dihydro-10-methoxy-9-methoxymethoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Structure 12 of Scheme IV, where X = S, PG = methoxymethoxy, $R^{13} = H$, $R^{14}R^{15} = \text{---}(\text{CH}_2)_5\text{---}$). Methoxymethyl ether (4.0 mL, 53 mmol) was added to a solution of Compound 140 (EXAMPLE 124) (4.0 g, 7.6 mmol) in dichloromethane (200 mL). Tetrabutylammonium hydroxide (1.0 [mL] mL) and a 6 M sodium hydroxide solution (1.0 mL) were added and the reaction solution stirred at room temperature for 1 h. The reaction was diluted with water (200 mL), the layers separated and the aqueous layer extracted with ethyl acetate (3 × 50 mL). The combined organic extracts were washed with 1 M hydrochloric acid (400 mL), a saturated solution of ammonium chloride (400 mL), dried (Na_2SO_4) and concentrated under reduced pressure. Purification by flash chromatography, eluting with ethyl acetate:hexanes afforded (Z)-5-(2'-(3'-piperidinecarbonylthienylmethylidene))1,2-dihydro-10-methoxy-9-methoxymethoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (3.6 g, 83 %) as a yellow oil.

Please replace the paragraph beginning on page 230, line 3 with the following amended paragraph:

(Z)-5-(2'-([3''])3'-Formylthienylmethylidene))-1,2-dihydro-10-methoxy-9-methoxymethoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Structure 18 of Scheme V, where X = S, PG = methoxymethoxy, $R^{13} = H$). This compound was prepared according to General Method 11 (EXAMPLE 167) from (Z)-5-(2'-(3'-hydroxymethylthienylmethylidene))-1,2-dihydro-10-methoxy-9-methoxymethoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline to afford (Z)-5-(2'-([3''])3'-formylthienylmethylidene))-1,2-dihydro-10-methoxy-9-methoxymethoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline.

Please replace the paragraph beginning on page 230, line 11 with the following amended paragraph:

(±)-(Z)-5-(2'-(3'-(1''-Hydroxy-2'',2'',2''-trifluoroethyl)thienylmethylidene))-1,2-dihydro-10-methoxy-9-methoxymethoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Structure 19 of Scheme V, where X = S, PG = methoxymethoxy, $R^{13} = H$, $R^A = \text{trifluoromethyl}$ trifluoromethyl). This compound was prepared according to General Method 15 (EXAMPLE 178) from (Z)-5-(2'-(3'-formylthienylmethylidene))-1,2-dihydro-10-

methoxy-9-methoxymethoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (EXAMPLE 167) and (trifluoromethyl)trimethylsilane to afford (\pm)-(Z)-5-(2'-(3'-(1''-Hydroxy-2'',2'',2''-trifluoroethyl)thienylmethylidene))1,2-dihydro-10-methoxy-9-methoxymethoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline.

Please replace the section on page 232, lines 8-10 with the following amended section:

(\pm)-(Z)-5-(4'-~~fluoro~~Fluoro-2'-(2'',2'',2''-~~Trifluoro~~trifluoro-1''-hydroxyethyl)benzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 206, Structure 45 of Scheme [[XI]] XII, where $R^3 = H$, $R^4 = F$, $R^5 = H$, $R^A = -CF_3$).

Please replace the paragraph beginning on page 233, line 18 with the following amended paragraph:

This compound was prepared according to General Method 8A (EXAMPLE 152) from (Z)-5-(2'-([3'']3'-formylthienylmethylidene))-1,2-dihydro-10-methoxy-2,2,4-trimethyl-9-(triisopropylsilyl)oxy-5H-chromeno[3,4-f]quinoline (EXAMPLE 167) and 4-fluoromagnesium bromide, followed by treatment according to General Method 12 (EXAMPLE 167) to afford Compound 208. 1H NMR (300 MHz, $CDCl_3$) δ 8.17 (d, $J=8.6$ Hz, 1H), 7.32 (dd, $J=8.5, 5.5$ Hz, 2H), 7.24 (d, $J=5.3$ Hz, 1H), 7.06 (d, $J=5.3$ Hz, 1H), 7.04 (d, $J=8.8$ Hz, 1H), 6.99 (t, $J=8.5$ Hz, 2H), 6.84 (d, $J=8.8$ Hz, 1H), 6.66 (d, $J=8.6$ Hz, 1H), 6.06 (s, 1H), 5.97 (s, 1H), 5.57 (s, 1H), 5.45 (s, 1H), 4.22 (s, 1H), 3.76 (s, 3H), 2.05 (s, 1H), 1.88 (m, 3H), 1.35 (s, 6H).

Please replace the section on page 234, lines 4-6 with the following amended section:

(\pm)-(Z)-5-(2'-(3'-(1''-Hydroxyallyl)thienylmethylidene))1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 209, Structure 20 of Scheme V, where $X = S$, $R^{13} = H$, $R^A =$ ~~1-hydroxyallyl~~ vinyl).

Please replace the paragraph beginning on page 234, line 22 with the following amended paragraph:

This compound was prepared according to General Method 8A (EXAMPLE 152) from (Z)-5-(2'-([3'']3'-formylthienylmethylidene))-1,2-dihydro-10-methoxy-2,2,4-trimethyl-9-(triisopropylsilyl)oxy-5H-chromeno[3,4-f]quinoline (EXAMPLE 167) and

cyclohexylmagnesium bromide, followed by treatment according to General Method 12 (EXAMPLE 167) to afford Compound 210. ¹H NMR (300MHz, CD₃OD) δ 8.31 (d, J=8.7 Hz, 1H), 7.27 (d, J=5.2 Hz, 1H), 7.02 (d, J=5.2 Hz, 1H), 6.92 (d, J=8.7 Hz, 1H), 6.74 (d, J=8.7 Hz, 1H), 6.73 (d, J=8.7 Hz, 1H), 6.07 (s, 1H), 5.50 (m, 1H), 4.47 (d, J=7.5 Hz, 1H), 3.76 (s, 3H), 2.05 (m, 3H), 1.81-1.53 (m, 5H), 1.31 (s, 6H), 1.25-0.86 (m, 6H).

Please replace the section on page 238, lines 10-12 with the following amended section:

(Z)-5-(2'-([3''])3'-(Cyclohexanecarbonyl)thienylmethylidene))1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 216, Structure 54 of Scheme XIV, where X = S, R¹³ = H, R^A = cyclohexyl).

Please replace the section on page 239, lines 16-18 with the following amended section:

(Z)-5-(2'-(3'-(Aminomethyl)thienylmethylidene))1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 218, Structure 33 of Scheme IX, where X = S, R¹³ = H, [[R¹⁹]] R¹⁴ = H, [[R²⁰]] R¹⁵ = H).

Please replace the section on page 240, lines 17-19 with the following amended section:

(Z)-5-(2'-(3'-(Phenylaminomethyl)thienylmethylidene))1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 219, Structure 33 of Scheme IX, where X = S, R¹³ = H, [[R¹⁹]] R¹⁴ = H, [[R²⁰]] R¹⁵ = phenyl).

Please replace the paragraphs on page 241, lines 3-15 with the following amended paragraphs:

(Z)-5-(2'-(3'-(Prop-2''-ynylaminomethyl)thienylmethylidene))1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 220, Structure 33 of Scheme IX, where X = S, R¹³ = H, [[R¹⁹]] R¹⁴ = H, [[R²⁰]] R¹⁵ = propyn-2-yl).

This compound was prepared according to General Method 16 (EXAMPLE 193) from (Z)-5-(2'-([3''])3'-formylthienylmethylidene))-1,2-dihydro-10-methoxy-2,2,4-trimethyl-9-(triisopropylsilyl)oxy-5H-chromeno[3,4-f]quinoline (EXAMPLE 167) and propargylamine, followed by treatment according to General Method 12 (EXAMPLE 167) to afford Compound 220. ¹H NMR (500MHz, Acetone-d₆) δ 8.30 (d, J=8.8 Hz, 1H), 7.32 (d,

J=5.1, 0.6 Hz, 1H), 7.04 (d, J=5.1 Hz, 1H), 6.99 (d, J=8.8 Hz, 1H), 6.80 (d, J=8.8 Hz, 1H), 6.79 (d, J=8.8 Hz, 1H), 6.31 (d, J=0.6 Hz, 1H), 5.86 (s, 1H), 5.56 (q, J=1.2 Hz, 1H), 3.86 (s, 2H), 3.77 (s, 3H), 3.38 (d, J=2.4 Hz, 2H), 2.64 (t, J=2.4 Hz, 1H), 2.08 (d, J=1.2 Hz, 3H), 1.34 (s, 6H).

Please replace the section on page 241, lines 18-21 with the following amended section:

(Z)-5-(2'-(3'-((2'',2'',2''-Trifluoroethylamino)methyl)thienylmethylidene))1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline ((Compound 221, Structure 33 of Scheme IX, where X = S, R¹³ = H, [[R¹⁹]] R¹⁴ = H, [[R²⁰]] R¹⁵ = 2,2,2-trifluoroethyl).

Please replace the section on page 242, lines 8-11 with the following amended section:

(Z)-5-(2'-(3'-(Cyclopropylaminomethyl)thienylmethylidene))1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 222, Structure 33 of Scheme IX, where X = S, R¹³ = H, [[R¹⁹]] R¹⁴ = H, [[R²⁰]] R¹⁵ = cyclopropyl).

Please replace the section on page 243, lines 1-3 with the following amended section:

(Z)-5-(2'-(3'-(1''-Butylaminomethyl)thienylmethylidene))1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 223, Structure 33 of Scheme IX, where X = S, R¹³ = H, [[R¹⁹]] R¹⁴ = H, [[R²⁰]] R¹⁵ = butyl).

Please replace the paragraph beginning on page 247, line 1 with the following amended paragraph:

(Z)-5-(2'-(3'-(Trifluoroacetyl)thienylmethylidene))1,2-dihydro-10-methoxy-9-methoxymethoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Structure 21 of Scheme V, where X = S, R¹³ = H, R^A = trifluoromethyl) was prepared according to General Method 11 (EXAMPLE 167) from (±)-(Z)-5-(2'-(3'-(1''-hydroxy-2'',2'',2''-trifluoroethyl)thienylmethylidene))1,2-dihydro-10-methoxy-9-methoxymethoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (EXAMPLE 178) to afford (Z)-5-(2'-([3'']₃'-(trifluoroacetyl)thienylmethylidene))1,2-dihydro-10-methoxy-9-methoxymethoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline.

Please replace the paragraph beginning on page 248, line 19 with the following amended paragraph:

[[A]] To a solution of (Z)-5-(2'-(3'-((E)-hydroxyiminomethyl)thienylmethylidene))-1,2-dihydro-10-methoxy-2,2,4-trimethyl-9-(triisopropylsilyloxy)-5H-chromeno[3,4-f]quinoline (EXAMPLE 167) (25 mg, 0.04 mmol) in 2 mL of anhydrous THF was added 1,1'-carbonyldiimidazole (65 mg, 0.40 mmol) under nitrogen. The solution was heated to reflux for 2 hrs then allowed to cool to room temperature. The mixture was extracted with ethyl acetate (25 mL) and water. The organic layer was washed with brine, dried over magnesium sulfate, filtered, and concentrated. Flash chromatography (ethyl acetate:hexanes) afforded Compound 231. ¹H NMR (500MHz, Acetone-d₆) δ 8.41 (d, J=8.7 Hz, 1H), 7.94 (s, 1H), 7.55 (dd, J=5.3, 0.7 Hz, 1H), 7.30 (d, J=5.3 Hz, 1H), 7.05 (d, J=8.7 Hz, 1H), 6.91 (d, J=8.7 Hz, 1H), 6.87 (d, J=8.7 Hz, 1H), 6.35 (d, J=0.7 Hz, 1H), 6.06 (s, 1H), 5.58 (q, J=1.3 Hz, 1H), 3.80 (s, 3H), 2.08 (d, J=1.3 Hz, 3H), 1.34 (s, 6H).

Please replace the section on page 249, lines 9-11 with the following amended section:

(Z)-5-(2'-(3'-Carbamoylthienylmethylidene))1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 232, Structure 30 of Scheme VIII, where X = S, R¹³ = H, R¹⁹, R²⁰, R¹⁴, R¹⁵ = H).

Please replace the paragraph beginning on page 249, line 26 with the following amended paragraph:

(Z)-5-(2'-(3'-Carbamoylthienylmethylidene))1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 232, Structure 30 of Scheme VIII, where X = S, R¹³ = H, R¹⁹, R²⁰, R¹⁴, R¹⁵ = H). To a solution of the (Z)-5-(2'-(3'-carboxythienylmethylidene))1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (20 mg, 0.04 mmol) in 2 mL of anhydrous DMF was added 1-hydroxybenzotriazole hydrate (12 mg, 0.09 mmol), ammonium chloride (5 mg, 0.09 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (17 mg, 0.09 mmol), and diisopropylamine (0.03 mL, 0.17 mmol). It was allowed to stir at room temperature for 14 hrs under nitrogen atmosphere. The mixture was then extracted with ethyl acetate (25 mL) and water. The organic layer was washed with brine, dried over magnesium sulfate, filtered, and concentrated. Flash chromatography (1:1 hexanes:ethyl acetate) afforded 12 mg (60%) of

Compound 232. ¹H NMR (500MHz, Acetone-d₆) δ 8.31 (d, J=8.7 Hz, 1H), 7.80 (s, 1H), 7.40 (d, J=5.4 Hz, 1H), 7.37 (dd, J=5.4, 0.6 Hz, 1H), 7.11 (s, 1H), 7.02 (d, J=8.7 Hz, 1H), 6.81 (d, J=8.7 Hz, 1H), 6.81 (d, J=8.7 Hz, 1H), 6.41 (s, 1H), 5.89 (s, 1H), 5.50 (q, J=1.2 Hz, 1H), 3.77 (s, 3H), 2.07 (d, J=1.2 Hz, 3H), 1.33 (s, 6H).

Please replace the paragraph beginning on page 251, line 19 with the following amended paragraph:

A solution of Compound 162 (EXAMPLE 146), acetic anhydride (4 equiv) in pyridine was stirred until consumption of starting material. The reaction was partitioned between ethyl acetate and dilute HCl. The reaction was washed with water, brine, dried over sodium sulfate, and concentrated. Flash chromatography (ethyl acetate:hexanes) afforded Compound [[162]] 234. ¹H NMR (500MHz, CDCl₃) δ 8.22 (dd, J=8.5, 5.9 Hz, 1H), 8.18 (d, J=8.5 Hz, 1H), 7.12-7.05 (m, 2H), 6.80 (d, J=8.8 Hz, 1H), 6.78 (d, J=8.8 Hz, 1H), 6.70 (d, J=8.5 Hz, 1H), 5.77 (s, 1H), 5.57 (s, 1H), 5.50 (m, 1H), 5.04 (s, 2H), 4.21 (s, 1H), 3.79 (s, 3H), 2.12 (d, J=1.2 Hz, 3H), 2.06 (s, 3H), 1.34 (s, 6H).

Please replace the paragraph beginning on page 252, line 18 with the following amended paragraph:

This compound was prepared in a manner identical to Compound 233 (EXAMPLE 208) except (Z)-5-(2'-formylbenzylidene)1,2-dihydro-10-methoxy-2,2,4-trimethyl-9-(triisopropylsilyl)oxy-5H-chromeno[3,4-f]quinoline (EXAMPLE 169) was used as the starting material to afford Compound 236. ¹H NMR (500MHz, CDCl₃) δ 8.16 (d, J=8.5 Hz, 1H), 8.10 (dd, J=7.9, 0.9 Hz, 1H), 7.47 (m, 1H), 7.32 (m, 1H), 7.21 (m, 1H), 6.93 (dd, J=17.5, 11.0 Hz, 1H), 6.79 (d, J=8.8 Hz, 1H), 6.79 (d, J=8.8 Hz, 1H), 6.69 (d, J=8.5 Hz, 1H), 5.92 (s, 1H), 5.58 (dd, J=17.5, 1.4 Hz, 1H), 5.50 (q, J=1.2 Hz, 1H), 5.23 (dd, J=11.0, 1.4 Hz, 1H), 4.19 (s, 1H), ~~Peak 15~~ 2.13 (d, J=1.2 Hz, 3H), 1.35 (s, 6H).

Please replace the paragraph beginning on page 253, line 23 with the following amended paragraph:

This compound was prepared in a manner similar to Compound 236 (EXAMPLE 211) except (Z)-5-(2'-(3'-formylthienylmethylidene))-1,2-dihydro-10-methoxy-2,2,4-trimethyl-9-(triisopropylsilyl)oxy-5H-chromeno[3,4-f]quinoline (EXAMPLE 167), diethyl (cyanomethyl)phosphonate and 60% NaH in mineral oil in THF was used to afford the

cyanovinyl adduct. Subsequent treatment according to General Method 12 (EXAMPLE 167) afforded Compound 238. ¹H NMR (500MHz, CDCl₃) δ 8.23 (d, J=8.5 Hz, 1H), 7.38 (d, J=16.2 Hz, 1H), 7.26 (d, J=5.4 Hz, 1H), 7.15 (dd, J=5.4, 0.6 Hz, 1H), 7.04 (d, J=8.8 Hz, 1H), 6.87 (d, J=8.8 Hz, 1H), 6.73 (d, J=8.5 Hz, 1H), 6.12 (d, J=0.6 Hz, 1H), 5.65 (d, J=16.2 Hz, 1H), ~~Peak 10—~~ 4.29 (s, 1H), 3.78 (s, 3H), 2.06 (d, J=1.0 Hz, 3H), 1.39 (s, 6H).

Please replace the paragraph beginning on page 257, line 5 with the following amended paragraph:

This compound was prepared according to General Method 13 (EXAMPLE 170) from (Z)-5-(2'-(3'-(2'',2'',2''-trifluoro-1''-hydroxy-1''-(trifluoromethyl)ethyl)thienylmethylidene))1,2-dihydro-10-methoxy-9-methoxymethoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (EXAMPLE 204), NaH (60% mineral oil ~~dispersion dispersion~~), and iodomethane in THF to afford the corresponding methyl ether. This compound was then stirred in 10% HCl:methanol (10 mg starting material/1 mL solution) at rt for 3h. The reaction was diluted with water, extracted with ethyl acetate, and the combined organic layer was washed sequentially with saturated sodium bicarbonate and saturated ammonium chloride, dried over sodium sulfate, and concentrated under reduced pressure. Flash chromatography (ethyl acetate:hexanes) afforded Compound 243. ¹H NMR (500MHz, Acetone-d₆) δ 8.35 (d, J=8.8 Hz, 1H), 7.88 (s, 1H), 7.60 (dd, J=5.6, 0.7 Hz, 1H), 7.12 (d, J=5.6 Hz, 1H), 7.03 (d, J=8.8 Hz, 1H), 6.85 (d, J=8.8 Hz, 1H), 6.84 (d, J=8.8 Hz, 1H), 6.66 (d, J=0.7 Hz, 1H), 6.00 (s, 1H), 5.54 (q, J=1.2 Hz, 1H), 3.80 (s, 3H), 3.45 (s, 3H), 2.06 (d, J=1.2 Hz, 3H), 1.37 (s, 6H).

Please replace the section on page 260, lines 5-8 with the following amended section:

(Z)-5-(2'-(3'-(Hydroxyethylcarbonyl)thienylmethylidene))1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 248, Structure 30 of Scheme VIII, where X = S, R¹³ = H, [[R¹⁹]] R¹⁴ = H, [[R²⁰]] R¹⁵ = 2-hydroxyethyl).

Please replace the paragraph beginning on page 260, line 18 with the following amended paragraph:

(Z)-5-(2'-(3'-(Hydroxyethylcarbonyl)thienylmethylidene))1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 248, Structure 30 of

Scheme VIII, where $X = S$, $R^{13} = H$, $[[R^{19}]] \underline{R^{14}} = H$, $[[R^{20}]] \underline{R^{15}} = 2\text{-hydroxyethyl}$) was prepared according to General Method 17 from (Z)-5-(2'-(3'-carboxythienylmethylidene))1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (EXAMPLE 207) and 2-hydroxyethylamine to afford Compound 248. 1H NMR (500MHz, Acetone- d_6) δ 8.31 (d, $J=8.7$ Hz, 1H), 7.80 (s, 1H), 7.48 (s, 1H), 7.37 (d, $J=5.4$ Hz, 1H), 7.33 (d, $J=5.4$ Hz, 1H), 7.18 (s, 1H), 7.01 (d, $J=8.7$ Hz, 1H), 6.83-6.80 (m, 2H), 5.90 (s, 1H), 5.53 (m, 1H), 4.02 (m, 1H), 3.77 (s, 3H), 3.65 (m, 2H), 3.45 (m, 2H), 2.07 (m, 3H), 1.34 (s, 6H).

Please replace the section on page 261, lines 3-5 with the following amended section:

(Z)-5-(2'-(3'-Ethylcarbamoylthienylmethylidene))1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 249, Structure 30 of Scheme VIII, where $X = S$, $R^{13} = H$, $[[R^{19}]] \underline{R^{14}} = H$, $[[R^{20}]] \underline{R^{15}} = \text{ethyl}$).

Please replace the section on page 261, lines 16-20 with the following amended section:

(Z)-5-(2'-(3'-((R)-2''-(Carbomethoxy)pyrrolidinecarbonyl)thienylmethylidene))1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 250, Structure 30 of Scheme VIII, where $X = S$, $R^{13} = H$, $\underline{NR^{19}R^{20}} \underline{NR^{14}R^{15}} = (R)\text{-2-(carbomethoxy)pyrrolidine}$).

Please replace the section on page 262, lines 7-9 with the following amended section:

(Z)-5-(2'-(3'-(Piperazinecarbonyl)thienylmethylidene))1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 251, Structure 30 of Scheme VIII, where $X = S$, $R^{13} = H$, $\underline{NR^{19}R^{20}} \underline{NR^{14}R^{15}} = \text{piperazine}$).

Please replace the section on page 262, lines 19-22 with the following amended section:

(Z)-5-(2'-(3'-(4''-Oxo-piperidinecarbonyl)thienylmethylidene))1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 252, Structure 30 of Scheme VIII, where $X = S$, $R^{13} = H$, $\underline{NR^{19}R^{20}} \underline{NR^{14}R^{15}} = 4\text{-oxo-piperidine}$).

Please replace the paragraphs on page 263, lines 9-20 with the following amended paragraphs:

(Z)-5-(2'-(3'-(2'',2'',2''-Trifluoroethylcarbamoyl)thienylmethylidene))1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 253, Structure 30 of Scheme VIII, where X = S, R¹³ = H, [[R¹⁹]] R¹⁴ = H, [[R²⁰]] R¹⁵ = 2,2,2-trifluoroethyl).

This compound was prepared according to General Method 17 (EXAMPLE 223) from (Z)-5-(2'-(3'-carboxythienylmethylidene))1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (EXAMPLE 207) and 2,2,2-trifluoroethylamine. ¹H NMR (500MHz, Acetone-d₆) δ 8.32 (d, J=8.7 Hz, 1H), 7.98 (t, J=6.2 Hz, 1H), 7.81 (s, 1H), 7.41 (dd, J=5.4, 0.6 Hz, 1H), 7.38 (d, J=5.4 Hz, 1H), 7.18 (d, J=0.6 Hz, 1H), 7.02 (d, J=8.7 Hz, 1H), 6.82 (d, J=8.7 Hz, 1H), 6.82 (d, J=8.7 Hz, 1H), 5.91 (s, 1H), 5.52 (q, J=1.3 Hz, 1H), ~~4.11~~ 4.11 (dq, J=6.2, 9.4 Hz, 2H), 3.77 (s, 3H), 2.07 (d, J=1.3 Hz, 3H), 1.34 (s, 6H).

Please replace the section on page 264, lines 1-4 with the following amended section:

(Z)-5-(2'-(3'-(4''-Hydroxypiperidinecarbonyl)thienylmethylidene))1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 254, Structure 30 of Scheme VIII, where X = S, R¹³ = H, ~~NR¹⁹, R²⁰~~ NR¹⁴R¹⁵ = 4-hydroxypiperidine).

Please replace the section on page 264, lines 13-16 with the following amended section:

(Z)-5-(2'-(3'-(4''-Methylpiperazinecarbonyl)thienylmethylidene))1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 256, Structure 30 of Scheme VIII, where X = S, R¹³ = H, ~~NR¹⁹, R²⁰~~ NR¹⁴R¹⁵ = 4-methylpiperazine).

Please replace the paragraph beginning on page 266, line 4 with the following amended paragraph:

(Z)-5-(2'-(3'-(3''-Hydroxy-3''-phenylpropanoyl)thienylmethylidene))1,2-dihydro-10-methoxy-9-(triisopropylsilyl)oxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Structure 50 of Scheme XIII, where X = S, R¹³ = H, R^G = Ph). Lithium bis(trimethylsilyl)amide (5 equiv,

THF solution) was added to a solution of (Z)-5-(2'-(3'-acetylthienylmethylidene))1,2-dihydro-10-methoxy-2,2,4-trimethyl-9-(triisopropysilyl)oxy-5H-chromeno[3,4-f]quinoline and benzaldehyde in THF at 0 °C. The reaction was quenched with saturated ammonium chloride, and extracted with ethyl acetate. The organic layer was washed with brine, dried over sodium sulfate, filtered, and concentrated. Flash chromatography (ethyl acetate:hexanes) afforded (Z)-5-(2'-(3'-(3''-hydroxy-3''-phenylbutanepropanoyl)-thienylmethylidene))1,2-dihydro-10-methoxy-9-(triisopropysilyl)oxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline.

Please replace the paragraph beginning on page 270, line 17 with the following amended paragraph:

For a discussion of the calculation of K_i , see *e.g.*, Cheng, Y. C. and Prusoff, W. H. *Biochem. Pharmacol.* 22:3099 (1973). K_i values for certain glucocorticoid binding compounds are shown in Table 1. The $[[K_i]]$ K_i values in Table 1 are provided as follows: A = < 1 nM, B = 1-2 nM, C = 2-3 nM and D = >3 nM.

Please replace the entry on page 271 in row 1, column 3 of Table 1 with the following amended entry:

$[[K_i]]$ K_i (nM)